REMARKS

Claims 19, 21-35, and 37-48 are pending without change.

On the Office Action Summary Page, the box for "This action is FINAL" and the box for "This action is non-final" are both checked. However, the conclusion to the Office Action does not have the form paragraphs for a Final Office Action and PAIR shows this Office Action to be non-final. Therefore, Applicants treat this Office Action as a non-final Office Action.

Applicants have reviewed the Examiner's objections and rejections set forth in the Office Action of April 4, 2008 and fully respond below.

Rejections under 35 U.S.C. § 103

Claims 19 and 21-35 , and 37-48 stand rejected under 35 U.S.C. § 103 for allegedly being obvious over Lord et al. (USP 6,417,227), WO 00/85162, or Diehl (USP 4,113,881) in view of IT-1302626. Applicants note that the Examiner listed the rejected claims as claims 19 and 21-48. Applicants respectfully submit that claim 36 was cancelled in a previous response and assume the listing of claims in the Office Action was a typographical error. Applicants further note that the cited International Application's correct publication number is WO 01/85162, as indicated on PAIR (Foreign Reference listed on 02-12-07). Applicants further assume that the incorrect citation was a typographical error, since WO 00/85162 does not exist.

In the Office Action, the Examiner reiterates her rejections of the claims based on the cited references as set forth in the Office Action of October 22, 2007. The Examiner alleges that it would have been obvious to extrapolate from the teaching of the references directed to the use of cetyl myristoleate for the treatment of arthritis (Lord and Diehl), or the use of certain cetylated fatty acids for the treatment of inflammatory bowel disease (WO 00/85162), to arrive at the claimed invention directed to the treatment of periodontal disease with cetylated fatty acids.

Applicants respectfully traverse for at least three reasons, which are discussed in detail below. First, Applicants submit additional evidence of failure of others for obtaining a successful anti-inflammatory treatment for periodontal disease in the Second Van Dyke Declaration, and argue that the Examiner's explanation in rejecting the First Van Dyke Declaration is not persuasive and is contrary to case law. Second, Applicants submit evidence in the Hasturk Declaration showing that the action of anti-inflammatory drugs is unpredictable. This evidence is consistent with the subject matter of a paper authored by Harry Diehl, the

inventor of the Diehl patent cited by the Examiner, submitted herewith and quoted below, which states not all cetylated fatty acids act similarly to treat inflammation. Third, Applicants submit evidence in the Spencer Declaration that the claimed invention enjoys commercial success.

1. Evidence of Failure of Others

The U.S. Supreme Court in *Graham v. John Deere*[1] has ruled that in obviousness analyses evidence of secondary considerations must be evaluated. The Supreme Court stated:

> Such secondary considerations as commercial success, *long felt but unsolved needs, failure of others*, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. (Emphasis provided.)[2]

The Court of Appeals for the Federal Circuit has used these secondary considerations to find claimed inventions non-obvious. For example, the Federal Circuit has stated:

> Finally, the record also suggests *that others in this market had tried to solve the need* for improved accuracy of the ultrafiltration monitors. The record reflects that those skilled in the art tried numerous, ultimately unsuccessful, solutions -- improving the electronics, improving the flowmeter technology, and recalibrating before dialysis. *This objective consideration also supports a conclusion of nonobviousness*. (Emphasis provided.)[3]

And elsewhere:

> A long felt but unsolved need for a workable resin based casting system is established by the attempts and failures of the major players in the casting field -- 3M, Bayer, Cutter, and JJO. All were attempting to develop a substitute for plaster based casting systems using fiberglass as the substrate, and all but 3M failed.[4]

The above is not an exhaustive listing of Federal Circuit cases in which failure of others rendered the claimed invention non-obvious. In fact, numerous other cases, too numerous to list, follow the rule of the Supreme Court and hold similarly.

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[1] *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966).

[2] Id. at ____.

[3] *Gambro Lundia AB v. Baxter Healthcare Corp.*, 110 F.3d 1573, 1580; 42 USPQ2d 1378, ___ (Fed. Cir. 1997). Invention related to dialysis devices.

[4] *Minnesota Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1574; 24 USPQ2d 1321, ___ (Fed. Cir. 1992). Invention related to plaster casts.

Applicants respectfully submit that they cannot understand the Examiner's reasoning against this legal backdrop. The Examiner has found the Van Dyke Declaration unpersuasive because it allegedly "still does not overcome the fact that the instant compounds are treating periodontal inflammation caused by the same pathway of inflammation in arthritis."[5] The Examiner states that

> In fact the declaration reiterates artisans have treated in the past to use anti-inflammatory compounds to treat periodontal inflammation. *The fact that those trials were unsuccessful does not render the instant method of treating periodontal inflammation unobvious*, especially since applicants are obviously treating the inflammation via the same pathway that the compounds use in treating arthritis. (Emphasis provided.)[6]

In effect, in stating the emphasized sentence above, the Examiner is stating that despite the rulings of the Supreme Court of the United States and the Court of Appeals for the Federal Circuit, the Examiner does not find that the failure of others is probative evidence of non-obviousness.

The Examiner goes on to say: "especially since applicants are obviously treating the inflammation via the same pathway that the compounds use in treating arthritis." Applicants respectfully submit that, if the Examiner's statement is taken as true, the Examiner has provided the quintessential case for where failure of others is sufficient evidence for non-obviousness. If, *arguendo*, Applicants are targeting the same pathway where others have failed, and Applicants are successful, then the invention must be non-obvious. Otherwise, others would have succeeded as well.

The Van Dyke Declaration provides ample evidence of long felt but unmet need and failure of others. Dr. Van Dyke explains that the use of anti-inflammatory drugs in general for the treatment of periodontal disease was suggested some time ago. However, currently there are no anti-inflammatory drugs for that use on the market and the practitioners do not use anti-inflammatory drugs for the treatment of periodontal disease.[7] The Examiner, on the other hand, does not provide any reasoning as to why the failure of others in this case is not persuasive. The Examiner's statement is conclusory and without any factual evidence to counter the facts set forth in the Van Dyke Declaration. Therefore, the Examiner's statement must be taken as a

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[5] The Office Action, page 3.
[6] The Office Action, page 4.

general statement against the probity of evidence of failure of others, as opposed to a statement against this particular case. Applicants respectfully submit that the Examiner's position in disregarding Applicants' evidence of the failure of others is legally untenable.

To provide further evidence for the failure of others in obtaining anti-inflammatory drugs that can be used to treat periodontal disease successfully and without adverse side effects, Applicants submit herewith the second declaration of Dr. Van Dyke. Dr. Van Dyke declares that at least two attempts have been made to perform clinical trials on anti-inflammatory drugs for the treatment of periodontal disease.

The first set of clinical trials was conducted on the drug flurbiprofen, which is being marketed under the trade name ANSAID® for the treatment of arthritis. Dr. Van Dyke declares that this program was abandoned because the manufacturer of flurbiprofen could not develop a dosing regimen with minimal side effects.[8]

The second drug to be tested for its efficacy in the treatment of periodontal disease was ketorolac, which is being marketed under the trade names TORADOL® and ACULAR® for pain management. Dr. Van Dyke declares "Phase III clinical trials failed to show efficacy and the program was abandoned."[9]

Dr. Van Dyke concludes that because others have tried, but have failed, to develop an anti-inflammatory drug for the treatment of periodontal disease, "to date there are no anti-inflammatory drugs in the market for the treatment of periodontal disease."[10]

Applicants respectfully submit that both the Van Dyke Declaration and the Second Van Dyke Declaration provide ample evidence of where others have tried but have failed to practice the claimed invention. Applicants further submit that, contrary to the Examiner's assertion that lack of success in others is not relevant, a host of case law, starting with holdings from the Supreme Court, hold that failure of others is evidence for the non-obviousness of a claimed invention. Therefore, Applicants respectfully request that the evidence of failure of others submitted herewith be reviewed favorably.

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[7] The Van Dyke Declaration, paragraphs 6 and 10.
[8] Second Van Dyke Declaration, Paragraphs 8-9.
[9] Second Van Dyke Declaration, Paragraph 10.
[10] Second Van Dyke Declaration, Paragraph 11.

2. Unpredictability of the Art

The instant claims are directed to the methods of using cetylated decanoic acid, cetylated lauric acid, cetylated myristic acid, cetylated palmitoleic acid, cetylated oleic acid, and cetylated stearic acid for the treatment of periodontal disease. In the case for the alleged unpatentability of the instant claims for being obvious, the Examiner cites references that teach the use of cetylated fatty acids not among the compounds of the claims, to treat diseases other than periodontal disease.

In her arguments for finding the present claims obvious, the Examiner cites two references that disclose the use of cetyl myristoleate for the treatment of arthritis (Lord and Diehl) and one reference disclosing other cetylated fatty acids for the treatment of inflammatory bowel disease (WO 00/85162) and concludes that "it would have been obvious to one of ordinary skilled [sic] in the art at the time the invention was made to *extrapolate* periodontal disease could be treated." (Emphasis provided.)[11] The Examiner continues:

> The compositions used in the [cited references] all treat inflammation, which is the source of the disease disclosed. Since it is known cetyl fatty acid containing compositions can be used to treat inflammation, it is obvious that these compositions cited will also treat periodontal disease cause [sic] by inflammation.[12]

For the reasons set forth below, Applicants respectfully submit that this line of reasoning is contrary to scientific findings. The action of anti-inflammatory drugs in inflammation pathways is unpredictable. This is especially true of the action of cetylated fatty acids. Some cetylated fatty acids inhibit the action of some inflammatory mediators, but not all cetylated fatty acids inhibit the action of all inflammatory mediators. Applicants respectfully show, below, that one cannot *a priori* predict with any expectation of success that one particular cetylated fatty acid will be effective in inhibiting one particular inflammatory mediator.

a. Declaration of Hasturk

Applicants have submitted herewith the declaration of Dr. Hatice Hasturk. Dr. Hasturk was a practicing periodontist and currently is an Assistant Professor at the Department of

[11] The Final Office Action, page 3.
[12] The Office Action, page 3.

Periodontology & Oral Biology at Boston University Goldman School of Dental Medicine. Dr. Hasturk is an expert in the field of periodontology.

Dr. Hasturk has studied the inhibition potential of various fatty acids, cetylated fatty acids, and mixtures thereof on monocyte-mediated cytokine release. The cytokines measured included all of the major inflammatory mediators, such as TNF-α, IL-1β, IL-6, IL-8, IL-12, and MCP-1. The methodology she used is described in detail in her declaration.[13] The compounds tested included 1-TDC, which is a blend of cetylated monounsaturated fatty acids, myristic acid, palmityl oleate, palmityl myristoleate, palmityl myristate, and cetyl myristate.

Figures 2-7 and Paragraphs 8-14 of the Hasturk Declaration show the results of the study. Dr. Hasturk discovered that the "data indicate that different compounds have different inhibitory effect on different inflammation mediators. A good inhibitor of one inflammation mediator may not have any effect at all on other inflammation mediators."[14] As an example, Dr. Hasturk points out that "cetyl myristate (CM) inhibits IL-8 80% by 24 hours (Fig. 6), shows some activity on the inhibition of TNF-α (Fig. 2) and MCP-1 (Fig. 7), but has no effect whatsoever on IL-1β (Fig. 3), IL-6 (Fig. 4), or IL-12 (Fig. 5)."[15]

In conclusion, Dr. Hasturk declares

> that positive results from inhibitory effects of one compounds in one inflammation pathway cannot be generalized to assume all anti-inflammatory compounds will be effective in all inflammation pathways. In other words, the effects of anti-inflammatory compounds in a particular inflammation pathway cannot be determined *a priori*. To determine whether a particular compound is effective in a particular inflammation pathway, the effect of that particular compound in that particular inflammation pathway should be studied experimentally.[16]

Applicants respectfully submit that the Hasturk Declaration clearly shows that knowing one cetylated fatty acid can have an inhibitory affect on one inflammatory mediator cannot lead one to predict, with any expectation of success, that the same cetylated fatty acid, or any other cetylated fatty acid, will also be effective in inhibiting another inflammatory mediator. These data show that the action of anti-inflammatory drugs on inflammation pathways is unpredictable.

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[13] Hasturk Declaration, Paragraph 5.
[14] Hasturk Declaration, Paragraph 15.
[15] Id.
[16] Hasturk Declaration, Paragraph 16.

The disclosure in the cited references that some cetylated fatty acids can be used to treat arthritis cannot, therefore, be used to predict that other cetylated fatty acids can be predicatively and successfully used to treat periodontal disease.

As discussed below, the findings of the Hasturk Declaration are consistent with the state of the art even before the priority date of the captioned application.

b. The Diehl Paper

Applicants have submitted herewith in an Information Disclosure Statement a journal article authored by Harry W. Diehl ("the Diehl paper")[17], who is also the inventor of USP 4,113,881 cited by the Examiner. The Diehl paper studies the effectiveness of cetyl myristoleate as a protection against the induction of arthritis in rats. The Diehl paper also reports the results of similar studies conducted on three other cetylated fatty acids, namely cetyl myristate, cetyl oleate, and cetyl elaidate.

The results are presented and discussed on page 298 of the Diehl paper. In pertinent part, it states:

> Analogues of cetyl myristoleate were also tested for their ability to retard or prevent adjuvant-induced arthritis in rats. Tested were the saturated ester, cetyl myristate, and two homologues [cetyl oleate, having the same 9-10 position of its *cis* (*Z*)-double bond as present in cetyl myristoleate; and cetyl elaidate, the *trans* (*E*)-isomer corresponding to cetyl oleate] In very limited preliminary trials, *only cetyl oleate had any significant activity, though much less than cetyl myristoleate . . . . A 1:1 mixture of cetyl oleate and cetyl myristoleate . . . gave results not greatly different from cetyl myristoleate alone* . . . . [¶,¶,¶] In conclusion, it is apparent that *cetyl myristoleate alone, of the four fatty acid esters tested, gave virtually complete protection* against adjuvant-induced arthritis in rats . . . . (Emphasis provided.)[18]

The Diehl paper, therefore, teaches that not all cetylated fatty acids are efficacious against arthritis. Even compounds that are structurally very similar, such as the ones studied in the Diehl paper, can have very different effects.

The Diehl paper shows that those of ordinary skill in the art cannot extrapolate from the therapeutic efficacy of cetyl myristoleate in the treatment of arthritis to the therapeutic efficacy

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[17] Diehl, H.W., Everette, L.M. "Cetyl Myristoleate Isolated from Swiss Albino Mice: An Apparent Protective Agent against Adjuvant Arthritis in Rats," *J. Pharm. Sci.* **1994**, *83:3*, 296-99.

[18] The Diehl paper, page 298, right-hand column.

of other cetylated fatty acids or all cetylated fatty acids. Therefore, the therapeutic efficacy of cetylated fatty acids for the treatment of arthritis appears to be unpredictable.

The Examiner suggests that it would be obvious to make a *double extrapolation*, to wit: we can extrapolate from cetyl myristoleate that other cetylated fatty acids are effective, and we can extrapolate from the treatment of arthritis to the treatment of periodontal disease. Applicants respectfully submit that the Diehl paper and the Hasturk Declaration conclusively show that this double extrapolation is improper. If in the treatment of a single disease, arthritis, one cannot extrapolate from one cetylated fatty acid to another to predict efficacy, then it would be completely impossible to make a double extrapolation of changing the compound *and* changing the disease.

Applicants respectfully submit that the Hasturk Declaration and the Diehl paper are evidence of unpredictability in this area. One of ordinary skill in the art cannot predict or extrapolate based on the efficacy of one compound in the treatment of one disease to the efficacy of another compound for the treatment of another disease. The Hasturk Declaration and the Diehl paper suggest that there is no expectation of success when a different compound is used for the treatment of the same disease. Consequently, Applicants respectfully submit that there is no expectation of success from the cited references for the use of a different compound for the treatment of a different disease.

3. Commercial Success

Applicants have submitted herewith the declaration of William P. Spencer, the inventor of the above-captioned application and Chief Executive Officer of Imagenetix, Inc., the assignee of the above-captioned patent application. Mr. Spencer states that he has had experience with obtaining funding for the company's various projects and understand that investors do not commit to investing on a project unless, through their due diligent analyses, they have determined that "the ensuing product is substantially more superior to any potentially competing product."[19] Mr. Spencer further declares that several investors have committed to investing in

[19] Spencer Declaration, Paragraph 8.

Imagenetix for the purpose of funding the clinical trials for the treatment of periodontal disease using the methods of the instant claims.[20] according to Mr. Spencer,

> [the investors] have come to the conclusion that the treatment methods encompassed by the methods claimed in the above-captioned patent application are commercially significant, are more superior to anything else that is currently available in the market or is in the pipeline of other pharmaceutical companies, and will likely be approved by the FDA.[21]

Mr. Spencer further declares that the investor interest in this project is the result of the investors' analyses of the treatment methods and had nothing to do with the marketing or commercialization of this project.[22] Further, Mr. Spencer establishes a nexus between the success of attracting investors and the merits of the claimed invention. Mr. Spencer declares that "our committed investors reached their decision after their thorough analysis of the pre-clinical data showing successful treatment of periodontal disease using the claimed methods."[23]

Applicants respectfully submit that the evidence of committed interest from investors in a claimed invention is evidence of commercial success of the claimed invention. Since the U.S. Supreme Court has held that evidence of commercial success is among the secondary indicia of non-obviousness, Applicants respectfully submit that the evidence of the Spencer Declaration is highly probative of the non-obviousness of the claimed subject matter. Investors, who are highly sophisticated businesspersons, would not invest their funds in the claimed subject matter if they were of the opinion that the claimed subject matter is so obvious that others would be entering the market and dilute their investment returns.

4. The claims are non-obvious

Applicants respectfully submit that for the reasons stated above, the pending claims are not obvious in view of the cited references. First, the Second Van Dyke Declaration provides evidence of failure of others where others have tried. The Examiner has dismissed similar evidence without comment or without providing contrary evidence. To rebut Applicants' evidence the Examiner must provide a reasoned analysis, which is lacking in the Office Action.

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[20] Spencer Declaration, Paragraph 7.
[21] Id.
[22] Spencer Declaration, Paragraph 9. *See*, *Gillette Co. v. S.C. Jounson & Son, Inc.*, 919 F.2d 720, 16 USPQ2d 1923 (Fed. Cir. 1990).
[23] Spencer Declaration, Paragraph 9.

Second, the Hasturk Declaration show that not all anti-inflammatory compounds affect the different inflammatory pathways similarly, while the Diehl paper shows that not all cetylated fatty acids are effective in the treatment of an inflammatory disease, arthritis. Therefore, there is not motivation in the art to use a cetylated fatty acid, whose efficacy is not known, to treat a disease that is arguably inflammatory. Third, the Spencer Declaration provides evidence of commercial success in the form of commitment by investors to invest in the assignee company to conduct clinical trials to obtain FDA approval for the claimed methods.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. § 103.

CONCLUSION

No claim is cancelled nor is any new claim added. Accordingly, claims 19, 21-35, and 37-48 are remain pending.

Applicants have endeavored to respond to all of the Examiner's objections and rejections set forth in the Office Action of April 4, 2008. Applicants respectfully submit that the claims are patentable and request a notice to that effect.

Applicants have submitted herewith a payment of $405 for a Request for Continued Examination (RCE) (small entity). If this fee is incorrect, Applicants request that the Director charge any additionally required fees, including any additional fees for an extension of time, or credit any overpayments to Deposit Account No. 50-4536. Applicants invite the Examiner to call the undersigned if any issue can be resolved through a telephonic discussion.

Respectfully submitted,

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